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EXAMINER

LIU, HONG

ART UNIT PAPER NUMBER

1624

DATE MAILED: 03/21/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/777,727

Applicant(s)

Platz et al.

Examiner

Hong Liu

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on _____
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 35 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-63 is/are pending in the application.
- 4a) Of the above, claim(s) 1-38 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 39-63 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirements.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- *See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892) 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 19) ☐ Notice of Informal Patent Application (PTO-152)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 1 & 5 & 6 20) ☐ Other:

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DETAILED ACTION

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-38, drawn to methods of using the compounds, classified in class 435, subclass 2.

II. Claims 39-63, drawn to the compounds, classified in class 544, subclass 251.

2. The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case more than one use exists for compounds of Group I as evidenced by claims 1-38 drawn to a variety of diverse uses. Additionally, the various uses would raise issues of enablement separate from that of the compound claims and would require art-recognized evidence that activity relied on its reasonably correlated to in vivo efficacy for the uses claimed.

If Group I is elected, further restriction may be required by the examiner.

3. During a telephone conversation with Ms. Susan Doughty on 03/04/02 a provisional election was made with traverse to prosecute the invention of Group II, claims 39-63.

Affirmation of this election must be made by applicant in replying to this Office action. Claims 1-

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38 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

4. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 39-60 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The following reason(s) apply:

The claims are not commensurate in scope as to the possibilities for the substituent "straight chain or cyclic saccharides," "amino acid groups," "alkylating Agents," "substituents that cause the compound to be substantially nonreactive to microorganisms..." in the various R definitions. They are open-ended and all encompassing. The specification does not enable any

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person skilled in the art to make and use the invention commensurate in scope with these broad claims, which embrace a diversity of substituents at various locations on the isoalloxazine ring.

In evaluating the enablement question, several factors are to be considered. Note In re Wands, 8 USPQ2d 1400 and Ex parte Forman, 230 USPQ 546. The factors include: 1) the nature of the invention, 2) the state of the prior art, 3) the predictability of lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

The nature of the invention in the instant application has claims which embrace a diversity of chemically and physically distinct compounds, wherein R1, R2, R3, R4, R5, and R6 is an optionally substituted straight or cyclic saccharide, amino acid groups, alkylating Agents, etc. While 3 or 4 compounds are disclosed, there is insufficient guidance for preparing additional isoalloxazine derivatives which would be effective in neutralizing biological contaminants since the cited examples are drawn to a homogenous group of compounds not remotely commensurate in scope to applicants' claims. Only compounds wherein R1 and R5 are methyl, R2, R3, and R6 is H, R4 is C(O)OR, N(CH)₂W(CH)₂Cl have been made.

Furthermore, no testing results are provided for any of the compounds listed in the specification. Examples should be of sufficient scope as to justify the scope of the claim. However, the generic claims are much broader in scope than is represented by the testing. The definitions of the various R variables on the isoalloxazine ring system embrace many structurally divergent groups not represented at all in testing, since testing for the instant compounds is not

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seen in the specification. Markush claims must be provided with support in the disclosure when the “working examples” fail to include written description(s) which teach how to make and use Markush members embraced thereby in full, clear and exact terms. See *In re Fouch*, 169 USPQ 429.

This area of activity can be expected to be highly structure specific and unpredictable, as is generally true for chemically-based pharmacological activity. In view of the structural divergence in the claims, one skilled in the art could not reasonably extrapolate the activities of some of the claimed compounds to the other structurally divergent compounds embraced by the claims which have not been tested. In cases directed to chemical compounds which are being used for their physiological activity, the scope of the claims must have a reasonable correlation to the scope of enablement provided by the specification. See *In re Surrey* 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. No reasonable assurance has been made that the instant compounds as an entire class have the required activities needed to practice the invention. Thus, factors such as “sufficient working examples”, “the level of skill in the art” and “predictability” have been demonstrated to be sufficiently lacking in the instant case for the scope being claimed.

6. Claims 40-51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for one of R1, R2, R3, R4, R5, and R6 being neither methyl nor H, does not reasonably provide enablement for a plurality of R1, R2, R3, R4, R5, and R6 being neither methyl nor H. The specification does not enable any person skilled in the art to which it pertains, or with

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which it is most nearly connected, to practice the invention commensurate in scope with these claims. The specification only discloses compounds that one of R1-R6 is neither CH3 or H.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 39, 60, and 61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

8. 1). Claim 60 is vague and indefinite in that the metes and bounds of the “alkylating agents” are unknown.

2). The examiner does not understand the meaning of the last three lines of claim 39 on page 53. What are the substituents?

3). Claim 61 is vague and indefinite as it is unclear what are the substituents for R1-R6 which have the desired biological activity.

9.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 39, 49-53, and 58 are rejected under 35 U.S.C. 102(b) as being anticipated by Tyrakowska et al. (J. Photochem. Photobiol., 1993). Tyrakowska teaches the compound of the instant invention where instant R is $(CH_2)_{10}-H$ (see Scheme 1).

Claims 39, 49-53, and 58 are rejected under 35 U.S.C. 102(b) as being anticipated by Koziol et al. (Inst. Commod. Sci., 1991). Koziol teaches the compound of the instant invention where instant R is methyl and ribityl; R1 is H, Me, undecyl, octadecyl.

Claims 39, 49-53, and 58 are rejected under 35 U.S.C. 102(b) as being anticipated by Schoo et al. (Macromolecules, 1992). Schoo teaches the compound of the instant invention (see Figure 5 on P. 1635).

Claims 39, 49-53, and 58 are rejected under 35 U.S.C. 102(b) as being anticipated by Herfeld et al. (Anti-Cancer Drug Des., 1998). The instantly claimed compounds read on the reference compound, see the enclosed copy of CAPLUS computer search report and the compounds having RN 144446-13-9 and 144446-14-0.

Claims 39, 49-53, and 58 are rejected under 35 U.S.C. 102(b) as being anticipated by Herfeld et al. (Lab. Chim. Ther., Fac. Sci. Pharm. Biol., 1994). The instantly claimed compounds read on the reference compound, see the enclosed copy of CAPLUS computer search report and the compounds.

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Claims 39, 49-53, and 58 are rejected under 35 U.S.C. 102(b) as being anticipated by Grimmer et al. (US 5,095,115). Grimmer teaches the compound of the instant invention wherein R1 is a phosphate group optionally substituted by a chlorine.

Claims 39, 49-53, and 58 are rejected under 35 U.S.C. 102(b) as being anticipated by Spencer et al. (US 3,920,650). Spencer teaches the compound of the instant invention wherein R3 is hydroxyethyl or R10 is phenyl (see table on Col. 7 and 8).

Claims 39, 49-53, and 58 are rejected under 35 U.S.C. 102(b) as being anticipated by Yagi et al. (US 3,189,598). Yagi teaches the compound of the instant invention (see Col. 1).

Claims 39, 49-53, and 58 are rejected under 35 U.S.C. 102(b) as being anticipated by Kuhn et al. (US 2,111,491). Kuhn teaches the compound of the instant invention wherein R1 is a phosphate group.

Claims 39, 49-53, and 58 are rejected under 35 U.S.C. 102(b) as being anticipated by Petering et al. (US 2,825,729). Petering teaches the compound of the instant invention (See Examples 1-42).

Claims 39, 49-53, and 58 are rejected under 35 U.S.C. 102(b) as being anticipated by Funk et al. (US 2,654,735). Funk teaches the compound of the instant invention wherein R1 contains a phosphate group (See Example 1 on Col. 4).

Claims 39, 49-53, and 58 are rejected under 35 U.S.C. 102(b) as being anticipated by Dickinson et al. 132: 10368. The instantly claimed compounds read on the reference compound, see the enclosed copy of CAPLUS computer search report and the compounds.

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Claims 39, 49-53, and 58 are rejected under 35 U.S.C. 102(b) as being anticipated by Herfeld et al. (Bioconjugate Chem., 1994). The instantly claimed compounds read on the reference compound, see the enclosed copy of CAPLUS computer search report and the compounds having RN 144446-18-4-9, 144446-17-3, .

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 39-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Spencer et al. (US 3,920,650). Spencer et al. teach a generic group of isoalloxazine derivatives (See formula I, Col. 1), in particular, where instant R3 is hydrogen, methyl, hydroxyethyl or benzyl, R7 is bromo, chloro, nitro, trifluoromethyl, R8 is hydrogen, butyl, phenyl, etc. In addition to Compounds I-XXVI which anticipate the claims as discussed in the above 102 rejection the reference compounds differ only in the nature of substituent for R3, R7, R8, and R10. However, the compounds of the instant invention are generically embraced by Spencer in view of the equivalence of hydrogen, phenyl bromo, propyl, etc. Thus, one of ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole. It has been held that a prior

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art disclosed genus of useful compounds is sufficient to render prima facie obvious a species falling within a genus. See *In re Susi*, 440 F.2d 442, 169 USPQ 423, 425 (CCPA 1971), followed by the Federal Circuit in *Merck & Co. V. Biocraft Laboratories*, 847 F.2d 804, 10 USPQ 2d 1843, 1846 (Fed. Cir. 1989).

Claims 39-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Petering et al. (US 2,825,729). Petering et al. teach a generic group of isoalloxazine derivatives (See formula I, Col. 1), in particular, where instant R1 is member selected from the (a), (b), and (c) substituents. In addition to Compounds which anticipate the claims as discussed in the above 102 rejection the reference compounds differ only in the nature of substituent for R1, R2, R3, and R5. However, the compounds of the instant invention are generically embraced by Spencer in view of the equivalence of acyloxy, sulfate, phosphate radicals, etc. Thus, one of ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole. It has been held that a prior art disclosed genus of useful compounds is sufficient to render prima facie obvious a species falling within a genus.

Claim Objections


Claims 62 and 63 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base

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claim and any intervening claims. None of the prior art of record nor a search in the pertinent art area teaches the exact species of the claims.

12. Any inquiry concerning this communication should be directed to Examiner Hong Liu whose telephone number is (703) 306-5814. If attempts to reach the examiner by the phone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached at (703) 308-4716. The fax phone number for this group is (703) 308-4734 for "unofficial" purposes and the actual number for **official** business is (703) 308-4556. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose number is (703) 308-1235.

Hong Liu
March 19, 2002


Mukund Shah
Supervisory Patent Examiner
Art Unit 1624